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10/528,021	07/29/2005	Helen Francis-Lang	EX03-067C-US	1018

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EXAMINER	
BERTOGLIO, VALARIE E	
ART UNIT	PAPER NUMBER
1632	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/528,021	FRANCIS-LANG ET AL.	
	Examiner	Art Unit	
	Valarie Bertoglio	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 November 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *1,3-16 and 18-28* is/are pending in the application.

4a) Of the above claim(s) *5,7-15 and 18-25* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-4,6,16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on *N/A* is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's election of Group III, claims 1-4,6,16 and 17 as they relate to use of a cell proliferation assay system in the reply filed on 02/08/2008 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 5, 7-15 and 18-25 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim.

Applicant's reply dated 11/24/2008 has been received. Claims 2 and 17 are cancelled. Claims 26028 are added. Claims 1,3-16 and 18-28 are pending. Claims 5, 7-15 and 18-25 are withdrawn. Claims 1,3-4,6, and 16 are under examination in the instant office action.

Specification

The use of the trademark TaqMan and RNeasy at page 37, for example, and has been noted in this application. It should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Applicant is advised that notice applies to use of any other trademarks that may be present throughout the specification, as well.

Claim Rejections - 35 USC § 112-1st paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1,3-4,6 and 16 remain rejected and newly added claims 26-28 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Applicant has performed a screen in Drosophila for genetic modulators of a phenotype caused by overexpression of Chk1, a gene that modulates the CHK pathway. The CHK pathway appears to be generically a term encompassing various cell-cycle checkpoints. The specification teaches that modulators of this global CHK pathway are referred to as PAKs (see page 3, lines 8-10). Applicant argues at page 13 of the Remarks dated 11/24/2008, that PAKS are not the same as Chk1 and are not considered to be "any" molecule that modulates Chk1 or the CHK pathway (page 13, lines 17-19). However, Applicant also states that PAK is the human ortholog of Chk1 (page 13, lines 21-23), thus PAK 'is' Chk1. Thus, the nomenclature used in describing the instant invention remains confusing, at best. However, it is now understood that Chk1 is considered a single *modulator* within the CHK system and the screen claimed is directed to identifying other such modulators. The specification defines PAKS as p21-activated kinases, refers to Chk1 as a PAK, yet fails to disclose any identifying characteristics to demonstrate that Chk1 is a p21-activated kinase. It is not clear to the Examiner if a modulator of the CHK pathway that is *not* a p21-activated kinase would be considered a PAK. PAK is considered here to be a member of the genus pf PAKs and other PAKS would have a name other than PAK.

In the Drosophila screen of the invention, Chk1 was overexpressed in the eye, leading to G2 cell cycle arrest and deterioration of eye morphology. Transposon insertion mutagenesis was used to screen for modulators of the phenotype. Modulators would be considered to act by modulating Chk1 and would be considered to be part of the Chk1 pathway. The chk1 gene, through this method, was found to enhance

the phenotype caused by overexpression of Chk1. The specification states that orthologs of the modifiers (i.e. chk1) are referred to as PAK. See page 34, last paragraph. The fly chk1 gene was found to have 52% amino acid identity with human p21-activated kinase Pak1 (see Genbank NP_002567). The specification fails to further characterize the transposon insertion into the chk1 gene that is reported to enhance the chk1 overexpression phenotype. An insertion that inactivates chk1, if anything, would be expected to suppress the chk1 overexpression phenotype.

The specification teaches that PAK RNAi knockdown resulted in decreased proliferation of MCF7 breast cancer cells. Thus, decreased PAK resulted in decreased proliferation, whereas overexpression of Chk1 in Drosophila resulted in cell cycle arrest. PAK overexpression in cells in vitro had no effect on colony growth, however some transcription factor expression was increased (paragraph bridging pages 38-39).

The specification fails to correlate the overexpression of chk1 in the drosophila eye to in vitro overexpression of PAK in mammalian cell culture. There appears to be inconsistencies in the effects of overexpression of chk1 in the fly, the enhancement of the overexpression phenotype by transposon insertion into the endogenous chk1 gene, and the effects of knockdown and overexpression of the human PAK homolog in cell lines.

That said; the claims are broad. While the specification is drawn to studies with a specific gene, chk1/PAK, the claims broadly encompass assaying using cells expressing any PAK, i.e. any modulator of the global CHK. The claims require expressing any PAK in cells, contacting the cells with an agent that modulates expression or activity of "a" PAK (i.e. the agent could modulate a PAK other than that of step (a)), wherein a difference in activity is detected in the presence of the agent. However, the specification fails to provide guidance relating to any PAK other than Chk1 and it's human homolog as set forth in SEQ ID NO:1. The skilled artisan would not know what agents modulate expression and/or activity of the PAK as required by the claims. Claim 3 requires the cell have defective CHK function. This is not

defined in the specification and could be any type of altered cell cycle regulation at all and may not involve p21 activated kinases.

The claims relate to identifying modulators of a "CHK" pathway. It is not defined what constitutes the "CHK" pathway. There are many signaling pathways involved in various cell cycle checkpoints. It is not known if all of these are considered to be part of the CHK pathway and it is not clear if the CHK pathway is intended to refer to a single signaling cascade or all checkpoint signaling pathways as a whole. The specification discusses a single genetic modulator screen and is extrapolating this to methods of screening for agents that affect any component that modulates any cell cycle checkpoint. The specification is not enabling for such broad extrapolation to unknown, unidentified, and uncharacterized signaling pathways and molecules.

Applicant's arguments have been fully considered and are not persuasive. Applicamt's remarks regarding the system claimed as defined by the specification are addressed above. Applicant also argues that all that is required under 35 USC 112 is that the specification describe the invention in terms to enable one of skill in the art to make and use the invention (Page 14). Applicant argues that the specification provides considerable guidance to enable the skilled artisan to make and use the claimed screening assays. Applicant argues that the specification teaches that PAK polypeptides and the HCK pathway are involved in cell cycle regulation and cell growth and that PAK polypeptides as p21 activated kinases involved in the regulation of cytosletal dynamics (page 15, paragraph 2). In response, this is all the guidance the specification provides. The specification provides no specific characterization or explanation how any specific PAK affects cell cycle control checkpoints. There is no relationship provided between Chk1, other PAKs and cytoskeletal dynamics. Not all cell cycle checkpoints act through the same mechanisms. Thus, it would require undue experimentation and characterization for one of skill in the art to use the claimed invention if they were to find an agent that binds a p21 activated kinase and leads to altered cell proliferation.

Applicant also argues that characteristics of PAK polynucleotides and polypeptides are described in detail in the specification at pages 4-7. However, the sequences provided are all related to the same PAK1 and generally discuss what homologs and/or orthologs are defined as and how such sequences *can* be derived or identified. The identity of no PAK other than PAK1 is provided and the mechanism of action is not provided for any PAK whatsoever. Given the support in the specification, the method as claimed amounts to no more than treating a cell with an agent and determining if cell proliferation (the elected assay of the invention) is affected.

Applicant argues that the specification discloses PAK modulating agents such as antibodies and antisense. However, the identity of the PAKs is not disclosed, the structure of the antibodies or antisense etc are not disclosed and their use is not known as the characteristics of the PAKs involved are not established. Thus, the specification fails to enable one of skill in the art to make and to use the invention as claimed.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Valarie Bertoglio whose telephone number is (571) 272-0725. The examiner can normally be reached on Mon-Thurs 5:30-4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras can be reached on (571) 272-4517. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Valarie Bertoglio/
Primary Examiner, Art Unit 1632